

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>GENENT.057QP</b>	<b>FOR FURTHER ACTION</b> <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. <b>PCT/US 00/ 12370</b>	International filing date (day/month/year) <b>05/05/2000</b>	(Earliest) Priority Date (day/month/year) <b>07/05/1999</b>
Applicant  <b>GENENTECH, INC. et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

3

☐ None of the figures.

## INTF NATIONAL SEARCH REPORT

International Application No

PCT/US 00/12370

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C12N15/12 C12N15/62 C07K14/505 C07K16/22  
G01N33/50 G01N33/53 A61K48/00 A61K38/18 A61P7/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, MEDLINE, STRAND, EMBL

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 94 24160 A (BRIGHAM &amp; WOMENS HOSPITAL) 27 October 1994 (1994-10-27) Note: 89.9 (89.4) % aa seq identity of monkey EPO with SEQ ID NO:2 (5) in 189 aa overlap, 86.9 % nt seq identity of cat EPO cDNA with SEQ ID NO:3 in 573 aa overlap. the whole document page 7, line 8 -page 8, line 12 example 1 page 55, table IV figure 6</p> <p style="text-align: center;">--- -/-</p>	1,8-15, 20,21

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

30 August 2000

Date of mailing of the international search report

15/09/2000

Name and mailing address of the ISA

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# INTERNATIONAL SEARCH REPORT

International Application No

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WEN D ET AL.: "Erythropoietin structure-function relationships: high degree of sequence homology among mammals" BLOOD, vol. 82, no. 5, 1 September 1993 (1993-09-01), pages 1507-1516, XP000938929</p> <p>Note: 90.2 (89.6) % aa seq identity of Macaca mulatta EPO with SEQ ID NO:2 (5) in 193 aa overlap.</p> <p>the whole document</p>	1,8,20, 21
X	<p>WO 95 05465 A (AMGEN INC) 23 February 1995 (1995-02-23)</p> <p>Note: 100 % aa seq identity of Asn57Thr59 EPO with SEQ ID NO:32.</p> <p>page 5, line 10-25 page 41, table 3, analog N9 page 56, table 6, Asn57Thr59 claims 1-8,10</p>	1,8-15, 20,21, 34-38
X	<p>EP 0 410 246 A (BEHRINGWERKE AG) 30 January 1991 (1991-01-30)</p> <p>the whole document</p>	28-33
X	<p>WO 95 13376 A (AMGEN INC ;UNIV SOUTHERN CALIFORNIA (US)) 18 May 1995 (1995-05-18)</p> <p>Note: 99.5 % aa seq identity of human EPO with SEQ ID NO:2 in 193 aa overlap, 99.5 % nt seq identity of human EPO cDNA with SEQ ID NO:3 in 585 nt overlap.</p> <p>page 38-40</p>	1,8-15, 20,21
X	<p>WO 85 02610 A (KIRIN AMGEN INC) 20 June 1985 (1985-06-20)</p> <p>Note: 91.2 (90.7) % aa seq identity of Cynomolgus monkey EPO with SEQ ID NO:2 (5) in 193 aa overlap.</p> <p>examples 3,10,12</p>	1,8-15, 20,21
A	<p>WO 99 02709 A (STROM TERRY B ;ZHENG XIN XIAO (US); BETH ISRAEL HOSPITAL (US); SYT) 21 January 1999 (1999-01-21)</p> <p>page 22, line 24 -page 29, line 7</p>	22,24, 36,38
P, X	<p>WO 00 24893 A (AMGEN INC) 4 May 2000 (2000-05-04)</p> <p>Note: 100 % aa seq identity of Asn55Thr57 EPO with SEQ ID NO:24.</p> <p>page 7, line 2-10 page 27, table 1, analog N54 claims 9,11,23-27</p>	1,8-15, 20,21, 34-38

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 28, 30(b), 31(b)

Remark (2): Present claims 28-32 relate to an extremely large number of possible CHEPO agonists and antagonists. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the antagonists claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to anti-CHEPO antibodies, as claimed in claims 30 and 33. Claim 28, and those parts of claims 30 and 31 where reference is made to agonists to a CHEPO polypeptide, have not been searched.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 00/12370

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark (1): Although claims 31-33 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 28, 30(b), 31(b)  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/12370

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9424160	A	27-10-1994	AU 6709794 A	08-11-1994
WO 9505465	A	23-02-1995	AT 155796 T	15-08-1997
			AU 677097 B	10-04-1997
			AU 7632794 A	14-03-1995
			CN 1105030 A	12-07-1995
			CZ 9500917 A	13-03-1996
			DE 69404401 D	04-09-1997
			DE 69404401 T	19-02-1998
			DK 640619 T	02-02-1998
			EP 0640619 A	01-03-1995
			ES 2105442 T	16-10-1997
			FI 951792 A	18-05-1995
			GR 3024815 T	30-01-1998
			HK 1001589 A	26-06-1998
			HU 72849 A	28-05-1996
			JP 11155584 A	15-06-1999
			JP 2938572 B	23-08-1999
			JP 8506023 T	02-07-1996
			LV 10972 A	20-12-1995
			LV 10972 B	20-10-1996
			NO 951445 A	16-06-1995
			NZ 273134 A	24-11-1997
			SI 640619 T	28-02-1998
			SK 50295 A	09-08-1995
			ZA 9406122 A	20-03-1995
EP 0410246	A	30-01-1991	DE 3924746 A	31-01-1991
			AT 161577 T	15-01-1998
			AU 648506 B	28-04-1994
			AU 5977890 A	31-01-1991
			CA 2021912 A	27-01-1991
			DE 59010787 D	05-02-1998
			ES 2111524 T	16-03-1998
			GR 3026096 T	29-05-1998
			JP 3081294 A	05-04-1991
			KR 175657 B	01-04-1999
			PT 94813 A,B	20-03-1991
			US 5712370 A	27-01-1998
			US 5106954 A	21-04-1992
WO 9513376	A	18-05-1995	AU 1095595 A	29-05-1995
			CA 2183551 A	18-05-1995
			EP 0737252 A	16-10-1996
WO 8502610	A	20-06-1985	US 4703008 A	27-10-1987
			AT 54940 T	15-08-1990
			AU 1007495 A	06-04-1995
			AU 657555 B	16-03-1995
			AU 2042192 A	08-10-1992
			AU 3612597 A	18-12-1997
			AU 600650 B	23-08-1990
			AU 3746785 A	26-06-1985
			AU 5272293 A	24-03-1994
			AU 5750490 A	04-10-1990
			AU 6981798 A	20-08-1998
			CA 1339047 A	27-05-1997
			CY 1643 A	14-05-1993

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/12370

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8502610 A		DE 3482828 D	30-08-1990
		DK 365185 A	11-10-1985
		EP 0148605 A	17-07-1985
		ES 538519 D	01-05-1988
		ES 8802329 A	16-07-1988
		HK 20093 A	19-03-1993
		IL 73785 A	15-11-1992
		IL 96581 A	13-05-1993
		IL 96582 A	04-04-1993
		IL 100935 A	04-04-1993
		JP 2708099 B	04-02-1998
		JP 8269096 A	15-10-1996
		JP 6093000 A	05-04-1994
		JP 7076239 B	16-08-1995
		JP 2957974 B	06-10-1999
		JP 10095799 A	14-04-1998
		JP 3017962 B	13-03-2000
		JP 10072366 A	17-03-1998
		JP 1055190 A	02-03-1989
		JP 2107224 C	06-11-1996
		JP 6055136 B	27-07-1994
		JP 1975769 C	27-09-1995
		JP 3198792 A	29-08-1991
		JP 4035159 B	10-06-1992
		JP 2655750 B	24-09-1997
		JP 3259098 A	19-11-1991
		JP 11253188 A	21-09-1999
		JP 2017156 B	19-04-1990
		JP 61501627 T	07-08-1986
		MX 9203598 A	01-09-1992
		NZ 210501 A	27-08-1991
		NZ 227326 A	27-08-1991
		NZ 227327 A	27-08-1991
		SG 92891 G	14-02-1992
		US 5955422 A	21-09-1999
		US 5441868 A	15-08-1995
		US 5756349 A	26-05-1998
WO 9902709 A	21-01-1999	AU 8182298 A	08-02-1999
WO 0024893 A	04-05-2000	AU 1124100 A	15-05-2000

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference GENENT.057QPC	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/12370	International filing date (day/month/year) 05/05/2000	Priority date (day/month/year) 07/05/1999
International Patent Classification (IPC) or national classification and IPC C12N15/11		
Applicant GENENTECH, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 8 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 5 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☒ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  01/12/2000	Date of completion of this report  23.07.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Trommsdorff, M  Telephone No. +49 89 2399 7361  



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/12370

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-91 as originally filed

**Claims, No.:**

1-42 as amended under Article 19

**Drawings, sheets:**

1/5-5/5 as originally filed

**Sequence listing part of the description, pages:**

1-23, filed with the letter of 24.07.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/12370

- ☐ the description,      pages:  
☐ the claims,      Nos.:  
☐ the drawings,      sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**II. Priority**

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:  
**see separate sheet**

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims	2-4, 9-15, 17, 22-24, 34-42
	No:	Claims	25-27
Inventive step (IS)	Yes:	Claims	
	No:	Claims	2-4, 9-15, 17, 22-27, 34-42
Industrial applicability (IA)	Yes:	Claims	2-4, 9-15, 17, 22-27, 34-42
	No:	Claims	

2. Citations and explanations  
**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/US00/12370

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**VI. Certain documents cited**

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/12370

**1. Cited documents**

The following documents (D) are referred to in this communication; the numbering is the same as in the search report and will be adhered to in the rest of the procedure:

- D1: WO 94 24160 A (BRIGHAM & WOMENS HOSPITAL) 27 October 1994 (1994-10-27)
- ✓ D2: WEN D ET AL.: 'Erythropoietin structure-function relationships: high degree of sequence homology among mammals' BLOOD, vol. 82, no. 5, 1 September 1993 (1993-09-01), p. 1507-16
- D3: WO 95 05465 A (AMGEN INC) 23 February 1995 (1995-02-23)
- D4: EP-A-0 410 246 (BEHRINGWERKE AG) 30 January 1991 (1991-01-30)
- D5: WO 95 13376 A (AMGEN INC; UNIV SOUTHERN CALIFORNIA (US)) 18 May 1995
- D6: WO 85 02610 A (KIRIN AMGEN INC) 20 June 1985 (1985-06-20)
- D8: WO 00 24893 A (AMGEN INC) 4 May 2000 (2000-05-04)

**2. Amendments**

The amendments filed with the International Bureau under Article 19(1) PCT do not introduce subject-matter which extends beyond the content of the application as filed and thus comply with Article 19(2) PCT. For the examination the claims have been renumbered from 1-26.

**3. Re Item II  
Priority**

The priority has been checked and appears to be valid. Thus, all claims enjoy the claimed priority date. Therefore, document D8 has not been considered to be part of the prior art as defined in the regulations (Rule 64(1)-(3) PCT).

**4. Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- 4.1. Claims 2-4, 9-15, 17, 22-24, 34-42 (renumbered 1-14 and 18-26) are directed to chimpanzee erythropoietin cDNA (with or without signal sequence), polypeptidic

sequences, analogs thereof, fusion proteins, vectors and host cells and methods for producing said polypeptides.

Several prior art documents disclose erythropoietin sequences from different species and analogs thereof. D1, for instance, compares the amino acid sequences of human, macaque, mouse, rat, sheep, pig and cat (Fig. 6). The chimpanzee erythropoietin amino acid sequence differs from the human sequence by only one amino acid at position 84. However, none of the prior art documents discloses chimpanzee erythropoietin cDNA or amino acid sequences. Thus, the subject-matter of said claims is novel (Art. 33(1) and (2) PCT).

- 4.2. Claims 25-27 (renumbered 15-17) are directed to antibodies which specifically bind to the claimed polypeptides.

D4 describes mono- and polyclonal antibodies against human erythropoietin produced by using synthetic peptides from human erythropoietin (p. 6-9, examples 1-9). Since human and chimpanzee erythropoietin only differ by one amino acid (most of the synthetic peptides used in D4 have the same sequence in human and in chimpanzee), antibodies directed against human erythropoietin will also recognize the chimpanzee protein. In fact, it would probably be impossible (and it is not shown by the applicants) to produce antibodies that specifically recognize the chimpanzee but not the human erythropoietin.

Hence, the subject-matter of claims 25-27 (15-17) lacks novelty (Art. 33(1) and (2) PCT).

- 4.3. Claims 2-4, 9-14, 17, 34, 35 and 39-42 (renumbered 1-9, 11, 18, 19 and 23-26) are directed to nucleic and amino acid sequences of the chimpanzee erythropoietin, analogs thereof, vectors and host cells comprising said polypeptides.

Prior art documents D1-D6 all disclose erythropoietin sequences and mutants thereof.

D1, for instance, discloses the amino acid sequences of erythropoietin from 8 different species (see above).

D5 also discloses the nucleic and amino acid sequences of human erythropoietin (Fig. 1 and p. 21, example 1).

The difference between D1 (or any of the prior art documents D2-D6) and the present application is the species from which the erythropoietin sequence is

isolated.

Thus, in view of D1, the problem to be solved is to identify further erythropoietin polypeptides which could be useful in the treatment of disorders of hematopoiesis. The solution proposed by the applicants is the identification of a chimpanzee erythropoietin and analogs thereof bearing mutations in the N- or O- glycosylation sites.

This solution cannot be considered as inventive for the following reasons: the isolation of the chimpanzee erythropoietin merely represents the identification of erythropoietin sequences from a further species. The sequence alignment shows that said chimpanzee protein is highly identical to already known erythropoietin proteins from other species (89.9% identity with the monkey protein, 90.2% identity with the Rhesus macaque protein and 99.5% identity with the human protein). Thus, since erythropoietin sequences of several species were known from the prior art, said chimpanzee erythropoietin can only be regarded as inventive, if said protein or the claimed analogs present unexpected effects or properties in relation to the other already known erythropoietin sequences. However, no such effects or properties are indicated in the application or can be expected since said protein differs from the human protein by only one amino acid. Moreover, the isolation of said sequence is technically easy and merely requires methods well-known in the art.

Hence, no inventive step is present in the subject-matter of claims 2-4, 9-14, 17, 34, 35 and 39-42 (renumbered 1-9, 11, 18, 19 and 23-26) (Art. 33(1) and (3) PCT).

The remaining claims 15, 22-27 and 36-38 (renumbered 10, 12-17 and 20-22) are directed to methods of producing said polypeptides, fusion proteins comprising said polypeptides and antibodies against said polypeptides. These are the standard applications the skilled person would have for any given protein and which involve standard methods well-known in the art. Hence, the subject-matter of said claims is also not inventive (Art. 33(1) and (3) PCT).

- 4.4. Claims 1-26 are considered to be industrially applicable in the field of pharmaceutical industry (Art. 33(1) and (4) PCT).

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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International application No. PCT/US00/12370

**5. Re Item VI**

**Certain documents cited**

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 00 24893 A	04.05.2000	18.10.1999	23.10.1998

The above cited document D8 discloses erythropoietin glycosylation variants, notably Asn55Thr57 erythropoietin, which is identical to seq. ID no 24 of the present application.

**6. Re Item VII**

**Certain defects in the international application**

- 6.1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D6 is not mentioned in the description, nor are these documents identified therein.
- 6.2. Claims 26 and 27 (renumbered 16 and 17) were read as referring to claim 25 (i.e. claim 15).

**7. Re Item VIII**

**Certain observations on the international application**

- 7.1. The term "about" used in claims 2, 4, 17, 40 and 41 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).
- 7.2. The content of table 1 (p.19-50) is unclear. This could be due to the format of said table which would need to be modified in order to be clear.